

## REMARKS

Applicants have amended the claims 11 and 24-29 to correct certain clerical errors. In particular, claim 11 has been amended to refer to the “x and y coordinates” rather than the “z and y coordinates.” Claims 24 – 29 have been amended to recite an “ordered array” rather than an “ordered redundant array,” to reflect previous amendments to their antecedent. Claims 11, 23, and 30 have also been amended to more clearly define the invention, by removing the recitation “wherein there is one copy of the sequence....” This amendment is supported by the original claims. Additionally, claims 11, 23 and 30 have been amended to make explicit that copies of the sequence of interest are at the terminus of the growing strand (i.e. the z dimension). These amendments are supported throughout the specification, particularly pages 5, 6, 20 and 21 and Figure 1A. As such, these amendments do not introduce new matter and their entry is respectfully requested.

The Examiner objected to certain informalities in claims 1 and 24-29. Applicants respectfully submit that the present amendments to the claims have obviated these objections, and respectfully request their withdrawal.

Claims 11 and 23-38 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

The Examiner has contended that the claims do not comply with the written description requirement on the basis of the following recitation: “wherein there is one copy of the sequence of the 3’ end of the original unextended oligonucleotide in the z dimension for each copy of the sequence of interest extending in the z dimension.”

Applicants respectfully disagree for the following reasons. First, applicants indicated in the Amendment filed January 14, 2005 that this amendment was supported at pages 10-11 of the specification, contrary to the Examiner’s assertion that no support was provided. Second, this claim recitation is supported throughout the specification. As explained at pages 10-11, the method taught by the invention uses a solid support with oligonucleotide probes immobilized at different positions, which are then extended by rolling circle amplification (RCA) using circular DNA templates to generate extended nucleic acid strands at each position of the solid support.

Anyone skilled in the art of rolling circle amplification knows that its product resembles a primer extension reaction product rather than a PCR amplification product, because it does not have a fixed end. Because it polymerizes continuously, the product of an RCA reaction is not a series of discrete nucleic acids of constant sizes, but instead is a linear nucleic acid with multiple copies of the sequence contained within the circular DNA. See page 4, line 20 – page 5, line 12 for a thorough explanation of the RCA reaction and its product.

Accordingly, applicants respectfully submit that the skilled artisan reading the specification would know that amplification of the starting, immobilized oligonucleotides with a circular template using RCA would generate a series of extended oligonucleotides, in which the 3' end of the starting oligonucleotide would be present in the final extended oligonucleotides  $n+1$  times, where  $n$  is the number of complete rounds of amplification of the circular template. Thus, if two complete rounds of amplification of the circular template occur, the final extended oligonucleotide would have three copies of this 3' end of the starting oligonucleotide. Applicants have attached a figure to more clearly illustrate the product of the RCA polymerization reaction. Applicants also note that there is no pre-determined position at which the RCA reaction terminates, but instead it can end at any point, as illustrated in attached figure.

While applicants disagree with the Examiner for all of the reasons stated here, applicants have amended the claims to expedite prosecution. In light of the above argument and the amendments to the claims, applicants respectfully submit that this rejection of the claims should be withdrawn.

Accordingly, in view of the foregoing, Applicants respectfully submit that all claims comply with 35 U.S.C. §112, first paragraph.

Claims 11 and 23-38 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants respectfully submit that the present amendments have obviated this rejection and respectfully request its withdrawal.

Accordingly, in view of the foregoing, Applicants respectfully submit that all claims comply with 35 U.S.C. §112, second paragraph.

Claims 11 and 23-38 were rejected under 35 U.S.C. §102(e) as being anticipated by Smith et al., U.S. Patent No. 5,753,439, filed May 19, 1998 ("Smith").

Applicants respectfully disagree and submit that the rejection should be withdrawn for the following reasons.

Claims 11 and 23 of the present invention are directed to arrays which are created by using rolling circle amplification to extend immobilized oligonucleotides, which serve as primers to amplify circular DNA templates containing a sequence of interest. Thus, in the final arrays the terminus in z dimension have many different extended immobilized oligonucleotides, where each extended immobilized oligonucleotide has multiple copies of the sequence of interest.

Claim 30 explicitly requires such redundancy at the terminus. Thus, the 3' terminus is part of the variable region. Whereas that 3' terminus in Smith is a constant region, as explained more fully below.

As previously explained, a fundamental difference between the claimed arrays and the Smith arrays is reflected in the 3' end of each immobilized oligonucleotides. Considering the entire array, there are two sources of variation in the present arrays: first, the sequence of the circular DNA template; and second, the point at which the RCA reaction terminates. For example, the extended immobilized oligonucleotides can be considered to have two sections: the original oligo coupled to the solid support, and the extended region, which is formed by amplification of the circular DNA template at the growing end, i.e., the z dimension. Thus, where a different circular DNA template hybridizes to different oligos immobilized at different x,y positions on an array, the 3' ends will necessarily differ, because the sequence of the circular DNA templates is different for each position. Second, as described in detail above, because RCA is an open-ended reaction, the end of the each extended immobilized oligonucleotide is not pre-determined, but will differ every time the same reaction is performed. Thus, even is one started with ten identical immobilized oligonucleotides and ten identical circular DNA templates, the RCA products, i.e. the extended immobilized oligonucleotides, would still all have different 3' ends, because the individual RCA reactions would end at different points along the sequence of the circular DNA template. In other words, the **3' ends of the final, extended oligonucleotides of the claimed arrays are highly variable.**

In contrast, the 5' and 3' ends of the Smith arrays are constant. The internal region is variable. This fundamental characteristic is acknowledged by the Examiner: "Each probe in the [Smith] array comprises a constant 5'-region, a **constant 3'-region** and a variable internal region..." (Page 5, lines 1-2 of 5/5/05 Office Action; emphasis added). Smith teaches that the 3' end of the probe is constant throughout the specification, including at col. 3, lines 22-23, and col. 9, lines 18-23. Claim 48 specifically claims an "array of at least 10 probes wherein **each probe** comprises ... an **identical 3' region**." Smith also specifies explicitly that the **3' region is about 15 – 100 nucleotides in length** (claim 11, e.g.). Taken together, Smith describes an array where the final 15 – 100 nucleotides of each probe on the array is identical, or constant. In contrast, as described above, the terminus, which includes the final 15 – 100 nucleotides of the extended immobilized oligonucleotides of the claimed arrays are part of the variable region. Thus, the Smith array in no way anticipates the present invention.

Accordingly, in view of the foregoing, Applicants respectfully submit that all claims comply with 35 U.S.C. § 102(e).

Claims 11 and 23 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,284,497 B1.


Applicants will file an executed terminal disclaimer separately.

Accordingly, in view of the foregoing, Applicants respectfully submit that all claims comply with

In view of the foregoing, applicants submit that all claims are in condition for allowance. Early and favorable action is requested.

Respectfully submitted,

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